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EXAMINER	
HIBBERT, CATHERINE S	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/849,498	YANG ET AL.	
	Examiner	Art Unit	
	Catherine S. Hibbert	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,8-16,44 and 49-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,8-16,44 and 49-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Amendments to the Claims and Amendments to the Specification, filed 24 October 2007, have been received and entered. Claims 2, 6-7, 17-43 and 45-48 are cancelled. Claims 49-53 are new. Claims 1, 3-5, 8-16, 44 and 49-53 are pending and under examination in this action.

Response to Arguments

The rejection under 35 U.S.C. 112, second paragraph, of cancelled Claim 2 is moot.

The rejection of claims 1, 3-4, 8-11 and 13-16 under 35 U.S.C. 102(b) as being anticipated by Schacht et al. is withdrawn herein based on Applicants Amendment to the claims filed 24 October 2007. The rejection of cancelled claim 2 is moot.

The rejection of claims 1, 3-4, 6, 8, 11 and 12 under 35 U.S.C. 102(b) as being anticipated by Wang et al. is withdrawn herein based on Applicants Amendment to the claims filed 24 October 2007. The rejection of cancelled claims 2 and 6 is moot.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 3-5, 8-16, and 44 stand rejected and newly added claims 49-53 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Lollo et al, (USPGPub 2003/0134420A1, filed 2 August 2002, published 17 July 2003, see whole document) for reasons of record and below. The rejection of cancelled claims 2, 6-7, and 48 is moot.

Applicants claim an article for delivering a drug and a nucleic acid, the article comprising: a nanoparticle forming a micelle; a nucleic acid associated with an exterior of the micelle; and a drug is associated with an interior of the micelle and a nucleic acid is associated with an exterior of the micelle (claim 1). Applicants further claim wherein the nucleic acid is DNA (claim 4), and wherein the article is in a composition with a pharmaceutically acceptable carrier (claim 10). Applicants also claim wherein the nanoparticle is capable of passing through a cell membrane, is stable at a concentration of greater than 5 mg/L, and comprises a graft co-polymer having a backbone including tertiary amines (at least a portion of the tertiary amines quarternized and bound to a hydrophobic side chain) (claims 3, 8 and 11). Applicants further claim limitations wherein the polymeric backbone comprises a copolymer of quaternized and non-

quaternized tertiary ammonium groups and wherein the polymeric backbone comprising a copolymer of quaternized and non-quaternized tertiary ammonium groups further comprises an ester linkage, a polyester, and a polyether (claims 13-16) and wherein the drug is not covalently or ionically bound to the nanoparticle (claim 52) and is physically contained by the nanoparticle (53).

Applicant provides a broad description in the specification for how molecules may be associated and dissociated with one another for the claimed invention. Applicant recites: "A first molecule may be "associated" with a second molecule, under set conditions, if the two molecules move together as a unit under these conditions. For example, the two molecules may be immobilized with respect to each other. The two molecules may be covalently or ionically bonded, may be joined by Van der Waal's forces or magnetic forces or one molecule may be physically contained or trapped by the second molecule or a collection of second molecules" [instant specification ¶ 0048]. Applicant further recites: "A first molecule may be "disassociated" from a second molecule or article with which it is associated. Disassociated means that the first molecule can move independently of the second molecule. The first molecule can also be disassociated from a second molecule or from an article if the second molecule or article degrades or is broken down so that it is no longer linked to the first molecule" [instant specification ¶ 0049].

In addition, applicants claim the article in claim 1 wherein the drug is a cancer drug and wherein the article is in a composition with a pharmaceutically acceptable carrier (claims 5 and 10). Applicants also claim a kit comprising: a container including

an amphoteric polymeric nanoparticle forming a micelle; a nucleic acid associated with an exterior of the micelle, a drug associated with an interior of the micelle; and instructions for administering the nanoparticle to a subject (claim 44).

Lollo et al teach a micelle complex comprised of amphoteric nanoparticles having a hydrophilic portion associating with DNA and/or cancer drugs and a hydrophobic portion capable of associating with cancer drugs and capable of passing through a cell membrane and capable of being directed to specific membranes by receptor-mediated targeting. In addition, Lollo et al contemplate a multidomain complex which can accommodate nucleic acids either on the interior or exterior and can accommodate drugs either on the interior or exterior (claims 49-52). For example, Lollo et al recite: "Typically, the center domain (Zone I of FIG. 1) contains the anionic agent. Examples of anionic agents include nucleic acids, negatively charged drugs and other small molecules capable of being delivered via a polyplex through a cellular boundary or lipid membrane" (¶ 0032, lines 2-4 and especially ¶ 0031-0038).

Furthermore, Lollo et al anticipate using their invention to treat a subject and although they do not explicitly recite "instructions", it would be inherent that any treatment plan for treating a human subject would inherently require instructions. For example, Lollo et al recite "A method for treating a subject comprising administering to said subject an effective amount of a penetration enhancer and a polyplex comprising a nucleic acid, a cationic backbone moiety, a hydrophobic moiety, and a hydrophilic moiety, such that said subject is treated" (Lollo et al claim 58, 59 and 68). Lollo et al

anticipate using the complex to deliver genes and drugs *in vivo* and thus anticipate claims 10 and 44.

Furthermore Lollo et al teach wherein the article forms a micelle and further teaches wherein a drug is associated with an interior of the micelle and a nucleic acid is associated with an exterior of the micelle (claims 1 and 44). For example, Lollo et al teaches partially hydrophobic conjugates also may be used since they possess moieties that preserve sufficient water solubility (since purely hydrophobic molecules are water insoluble). These conjugates can be made up of two different types of grafts, hydrophilic moieties to maintain adequate water solubility (`A`), and hydrophobic moieties (`B`) to introduce a domain with binding and micelle formation properties. In one embodiment, the polymer is designed by grafting two or more of these elements onto a cationic backbone moiety (e.g., a cationic polymer, `C`) (claims 49-51). A suitable grafting element, or hydrophilic moiety for this approach is PEG, which promotes solubility and steric shielding. Another suitable grafting element is any hydrophobic moiety, as described above, which may form domains with binding capabilities. These two or more types of grafting elements can then be randomly distributed along a cationic backbone moiety during the grafting step (¶ 0067, lines 1-6).

In addition, Lollo et al teaches an article as in claim 1 wherein the nanoparticle is stable at a concentration of greater than 5 mg/L because Lollo et al recites "polyplex concentration are reported by DNA content and were 10 ug/ml" which reads on the instant claim 8.

Furthermore, Lollo et al teach an article as in claim 1 wherein the nanoparticle comprises a graft co-polymer having a backbone including tertiary amines, at least a portion of the tertiary amines quaternized and bound to a hydrophobic side chain (claim 11), and further teaches wherein the hydrophobic side chain comprises cholesterol (claim 12). For example, Lollo et al teaches FIG. 11 shows the structure of grafted polymers with two hydrophobic domains per PEG chain. FIG. 11a shows a hydrophobic domain between the cationic domain and the surface domain. FIG. 11b shows a hydrophobic domain positioned at the terminus of a surface (e.g., hydrophilic) domain, and between the surface (e.g., hydrophilic) and cationic domains (¶ 0023, lines 1-3) (claims 49-53).

Therefore Lollo et al teach applicant's invention and anticipate claim limitations for claims 1, 3-5, 8-16, 44 and 49-53.

Applicant's response is that Lollo discloses methods and compositions for gene delivery and, in particular, polynucleotides (See Abstract). To accomplish such delivery, Lollo describes a polyplex including a nucleic acid (DNA) in a center region and functional moieties at a surface region (See FIG. 1, paragraph 32). Applicants submit that "in contrast, claims 1 and 44 have been amended to recite that a drug is associated with the interior of the micelle and nucleic acid associated with an exterior of the micelle" and that therefore "Lollo fails to teach or make obvious such an arrangement". Furthermore, Applicants state that "Lollo appears to rely on the nucleic acid being in the interior of the polyplex to facilitate its delivery, rather than at an exterior as claimed".

Therefore, Applicants conclude that "because each claim limitation is not taught or made obvious, claims 1 and 48" and remaining dependent claims are patentable over Lollo.

Applicants arguments have been fully considered and are respectfully found unpersuasive because Lollo et al teach wherein the article forms a micelle and further teach wherein a drug is associated with an interior of the micelle and a nucleic acid is associated with an exterior of the micelle (claims 1 and 44). For example, Lollo et al recite "the invention provides novel molecular complexes, referred to as "polyplexes" containing an anionic compound, such as a nucleic acid, associated with one or, more typically, multiple co-polymer domains, including a cationic domain, a transitional domain, and/or a surface domain (¶ 0005, lines 1-2).

> As shown in FIG. 1, polyplexes of the present invention are made up of multiple co-polymer domains. These domains are organized by the type of functional groups present on the co-polymer making up the domain. Typically, **the center domain** (Zone I of FIG. 1) contains the anionic agent. Examples of anionic agents include nucleic acids, **negatively charged drugs** and other small molecules capable of being delivered via a polyplex through a cellular boundary or lipid membrane. The cationic domain (Zone II of FIG. 1) is designed to interact, e.g., electrostatically, with the anionic domain/agent. Generally, the cationic domain is comprised of one or more cationic backbone moieties of copolymers, which are described in greater detail below. The transitional domain (Zone III of FIG. 1) links the cationic domain with the surface domain, typically via linear or branched co-polymers. The transitional domain may be hydrophobic in nature and may be comprised, at least in part, of hydrophobic moieties of copolymers. When the transitional domain is comprised at least in part of hydrophobic moieties, it is generally referred to as the "hydrophobic domain." Finally, the surface domain (Zone IV of FIG. 1) defines the polyplex surface by way of, for example, branching elements which allow the introduction of multiple molecules or other polymers on the polyplex surface. Such moieties modify the surface properties of the polyplex so as to enhance overall delivery of the anionic agent. The surface domain may be comprised, at least in part, of hydrophilic moieties of copolymers, as well as other ligands and other surface moieties which allow the polyplex to perform its intended function [0032].

Therefore, claims 1, 3-5, 8-16, 44 stand rejected and claims 49-53 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Lollo et al for reasons of record and above. The rejection of cancelled claims 2, 6-7, and 48 is moot.

New Grounds of Objection/Rejection

Claim Objections

Claims 4 and 5 are objected to because of the following informalities: Claims 4 and 5 are missing periods. Appropriate correction is required.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Catherine S. Hibbert whose telephone number is 571-270-3053. The examiner can normally be reached on Monday-Friday, 7:30 AM-5:00 PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully submitted,

Catherine S. Hibbert/AU1636